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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,201	12/19/2001	Gijs Van Rooijen	058187-0108	4943

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EXAMINER	
FOX, DAVID T	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,201	ROOIJEN ET AL.	
	Examiner	Art Unit	
	David T. Fox	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *3,5-7,9-14,17-19 and 21-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,8,15-16 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's amendments and arguments of 11 March 2004 have overcome the obviousness-type double patenting rejection and the indefiniteness rejection of record.

The petition under 37 CFR 1.53(e) of 25 July 2003 has been treated as a petition under 37 CFR 1.181(a) requesting acceptance of the paper filed with the petition as page 1 of the specification. The petition has been GRANTED per the Decision mailed 08 December 2003. The preliminary amendment to page 1 of the specification, filed 29 August 2002, has not been entered because it introduced no changes to page 1 of the specification as filed with the petition of 25 July 2003.

Applicant is reminded that claim 8, line 6 needs to be amended to insert ---is--- after "polypeptide", as stated on page 2 of the last Office action. See claim 8, line 4.

Claims 1-2, 4, 8, 15-6 and 20 remain objected to for reading on non-elected subject matter, and still need to be amended to reflect the elected subject matter of Group I, as stated on page 2 of the last Office action.

Applicant's arguments filed 11 March 2004 have been fully considered but they are not persuasive. Applicant urges that the Examiner has not demonstrated that a burdensome search would be needed to examine the claims in their current form, that the record provides no rationale for the species election urged by the Examiner, and that it is improper for the Examiner to elect a species for Applicant.

The Examiner maintains that searching both the plants of Group II and the animal or yeast cells of Group I, as encompassed by the generic claims of Group I,

would be an unduly burdensome search, since different culture and transformation methods are required by each, as stated on page 5 of the Restriction of 27 May 2003. The plant cells of Group II require Agrobacterium-mediated transformation, not required by the animal or fungal cells Group I. The plant cells of Group II are surrounded by a rigid cell wall, and would require enzymatic digestion thereof before electroporation- or polycation-mediated transformation, not required by Group I. Applicant elected Group I, namely animal or fungal cells versus the plant cells of Group II as recited on pages 3 and 5 of the Restriction mailed 27 May 2003, without traverse in the Election of 25 July 2003. Such election *without traverse* of animal or yeast cells versus plant cells clearly establishes on the record that these two types of transformants are restrictable. Additionally, the Examiner separated these types of transformants during the prosecution of commonly owned prior applications drawn to transformation with oil body protein-encoding genes, resulting in the issuance of U.S. Patent 5,650,554 drawn to transformed plant cells, and U.S. Patent 5,948,682 drawn to transformed yeast cells. Furthermore, Applicant's instant election without traverse of animal and yeast cells versus plant cells was a constructive election of that species as it pertained to the generic claims of Group I. Thus, the Examiner did not elect a species for Applicant, contrary to Applicant's assertions.

Claims 1-2, 4, 8, 15-16 and 20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention, as stated on pages 4-6 of the last Office action.

Applicant's arguments filed 11 March 2004 have been fully considered but they are not persuasive. Applicant points out the Examiner's erroneous statement in the last Office action that ferredoxin reductase enzymes are a type of thioredoxin reductase. Applicant further argues that the specification provides sequences for both thioredoxin and thioredoxin reductase genes, guidance for isolating substantially homologous sequences, the active sites for these two enzymes, and assays for determining whether fragments of the enzymes possess the activity of the entire enzyme.

The Examiner thanks Applicant for pointing out the typographical error on page 4 of the last Office action. Nevertheless, the Examiner maintains that Applicant's disclosure of a single species, namely NADPH thioredoxin reductase enzymes and genes encoding them, is insufficient to adequately describe the broadly claimed genus of any type of thioredoxin reductase enzyme and genes encoding it.

Regarding the provision of multiple sequences encoding multiple thioredoxin proteins, the Examiner does not dispute this, but maintains that no guidance has been provided for the characterization of a multitude of "active" *fragments* of these proteins. Regarding the provision of multiple sequences encoding multiple thioredoxin reductase proteins, the Examiner notes that all of these sequences encode a single type of thioredoxin reductase, namely *NADPH-* thioredoxin reductase, and that no guidance has been provided for the characterization of a multitude of "active" fragments of these proteins.

Regarding the alleged disclosure of active sites for each enzyme, the Examiner maintains that the active sites recited in the instant specification are too general and non-specific to be diagnostic for the claimed enzymes, and that the mere presence of these active sites would not be correlated with thioredoxin activity or thioredoxin reductase activity, as required by MPEP 2163. The active site of thioredoxin set forth on page 43 of the specification is an amino acid sequence of six residues which is only specifically characterized by the presence of cysteine at two residues. The other four amino acids are characterized as "any" amino acid (see page 43 of the specification, lines 18-25). The active site of thioredoxin reductase is the mere presence of a disulfide bond provided by two contiguous cysteine residues, surrounded by any other amino acid residues (see page 45 of the specification, lines 6-8). Neither of these sequences are unique to the claimed enzymes, and so neither of these sequences are correlated with thioredoxin activity or thioredoxin reductase activity.

Regarding the disclosure of methods for isolating homologous sequences or methods for assaying enzymatic fragments for activity, Applicant is directed to the following teaching:

An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product. Alternatively, disclosure of a method for producing a product does not *reduce to practice* the product itself. See *Bayer v. Housey*, Appeal No. 02-1598, (Fed. Cir. 2003), decided 22 August 2003, penultimate page: "processes of identification and generation of data are not steps in the manufacture of a final [drug] product". A product

that has not been reduced to practice cannot be described, as taught by *University of California v. Lilly* cited previously.

Claims 1-2 and 8 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to methods of transforming fungal or animal cells with constructs encoding fusion proteins comprising an oil body targeting protein linked to a thioredoxin or an NADPH thioredoxin reductase protein, does not reasonably provide enablement for claims broadly drawn to any method for somehow "associating" thioredoxin or thioredoxin reductase with oil body proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, as stated on pages 6-7 of the last Office action.

Applicant's arguments filed 11 March 2004 have been fully considered but they are not persuasive. Applicant urges that the enablement rejection is improper, given the failure of the Examiner to cite a publication specifically directed to oil body proteins, the widespread use of oil body proteins to target a variety of proteins as illustrated by references previously cited by Applicant, and the recitation in the specification of alternative ways of associating proteins.

The Examiner maintains that the cited publication demonstrates that the association of proteins in various tissues *in vivo* is generally unpredictable. Although success has been achieved using oil body proteins, that success *in vivo* has been limited to the expression of transgenes encoding the oil body proteins. Other types of association, such as the injection of biological tissues, cells or multicellular organisms

with whole proteins, followed by the localization of said proteins to the desired intracellular compartment or tissue type, have not been demonstrated by Applicant or the prior art, and no guidance has been provided for protein injection or alternate methods of protein association *in vivo*. The claims are drawn to methods of producing recombinant peptides *in a cell, followed by* protein association. The Examiner does not dispute that protein association occurs within cells, but maintains that the only type of production of protein within a cell demonstrated by Applicant or the prior art is the production of protein via the expression of transgenes encoding the protein.

Claim 20 remains rejected under 35 U.S.C. 102(b) as being anticipated by Ting et al, as stated on pages 7-8 of the last Office action.

Applicant's arguments filed 11 March 2004 have been fully considered but they are not persuasive. Applicant urges that the Examiner has failed to establish the inherency of the claimed subject matter as taught by the prior art.

The Examiner maintains that the claim is drawn to a product comprising a gene encoding a protein comprising an oil body protein operably linked to an "active fragment" of a thioredoxin or thioredoxin reductase protein. The specification provides no definition for what an "active fragment" entails. Is biological activity equivalent to the whole enzyme contemplated, or is mere antigenic activity contemplated? Furthermore, the claim as written encompasses active fragments of either the encoded protein or the gene encoding it. No definition is provided for what constitutes an active fragment of the gene. A single base pair or a single triplet codon can be said to be active, regarding

its involvement in the transcription of mRNA and the translation of an amino acid residue. Thus, the prior art teaches the claimed subject matter.

Furthermore, the prior art gene appears to be indistinguishable from a gene encoding a fusion protein comprising two different proteins, since the recitation of "active fragment" is so broad. The derivation of a gene fragment, including a single base pair or single triplet codon, from a non-oil body protein gene would not distinguish that fragment from the identical base pair or triplet codon found in an oil body protein gene. Thus, the prior art, which teaches a gene comprising an oil body protein gene, inherently comprises an active fragment of an oil body protein gene and an active fragment of some other gene encoding some other protein. The claim is not drawn to a process for producing a fusion protein-encoding gene comprising the isolation of sequences from two different proteins, followed by ligating fragments thereof.

See In re Best, 195 USPQ 430, 433 (CCPA 1977), which teaches that where the prior art product seems to be identical to the claimed product, except that the prior art is silent as to a particularly claimed characteristic or property, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention.

Claims 1-2, 4, 8 and 15-16 remain free of the prior art, as stated on page 8 of the last Office action.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (571) 272-0795. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

May 27, 2004

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638